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PASSIVE IMMUNIZATION AGAINST SAXITOXIN ADMINISTERED
INTRAVENOUSLY OR VIA THE RESPIRATORY TRACT

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In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council. The facilities are fully accredited by the American Association for Accreditation of Laboratory Animal Care.

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D.A. CREASIA and S.R. DAVIO. Passive Immunization Against Saxitoxin Administered Via the Respiratory Tract. Toxicon __, __, 19__. --In this study we compared the pulmonary and systemic toxicities of saxitoxin and examined the ability of anti-saxitoxin rabbit serum to protect mice from saxitoxin-elicited pulmonary toxicity. We found the 24-hr LD₅₀ for intratracheally instilled saxitoxin to be 11.2 µg/kg, while that for i.v. toxin was 11.7 µg/kg. When mice were treated with either intratracheal or i.v. saxitoxin at a dose of LD₅₀, a 1:2 dilution of rabbit anti-saxitoxin, injected i.p. 1 hr before toxin treatment, provided 100% protection.

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INTRODUCTION

Saxitoxin, one of the most lethal non-protein toxins known (DAVIO, 1985), is produced by dinoflagellates of the genus Gonyaulax (SUMNER et al., 1937; SCHANTZ et al., 1966). Gonyaulax dinoflagellates can contaminate shellfish, which, when eaten by humans, have been known to cause numbness, paralysis and death due to respiratory arrest. The primary therapy for saxitoxin poisoning in man is artificial respiration; there is no specific antidote accepted (HALSTEAD, 1967).

In a previous paper, DAVIO (1985) reported that anti-saxitoxin rabbit serum injected i.p. protected mice against the lethal effects of s.c. injected saxitoxin. However, the slower absorption kinetics of s.c. injected saxitoxin could have contributed to the protection afforded by the i.p. injected antiserum by allowing more time for interaction of toxin and antitoxin serum in the circulation. To test this, we passively immunized mice against saxitoxin by i.p. injection of anti-saxitoxin rabbit serum and challenged the mice 1 hr later by either i.v. injection or intratracheal instillation of saxitoxin. The results of these experiments are presented in this report.

MATERIALS AND METHODS

Saxitoxin

The saxitoxin used in this study was obtained from the Edgewood Arsenal, Aberdeen Proving Ground, MD.

RESULTS

Dose-response data comparing the lethality in mice of saxitoxin administered either intratracheally or i.v. are summarized in Table 1. Probit analysis of the data indicate that the LD_{50} for saxitoxin administered intratracheally was 11.2 ± 0.6 $\mu\text{g/kg}$ body weight, while that for i.v. injected saxitoxin was 11.7 ± 0.4 $\mu\text{g/kg}$. These LD_{50} values are similar and compare favorably with that previously reported by DAVTO (1965) for i.p. injected saxitoxin (12.9 ± 0.5 $\mu\text{g/kg}$). There were no discernible differences in time to death nor clinical signs of toxicity (data not presented) in any of the saxitoxin-treated mice that could be attributed to the route of administration.

When antiserum was administered to mice 1 hr before saxitoxin treatment, we found that antiserum dilutions of 1:1 and 1:2 offered complete protection against a lethal challenge dose of 20 $\mu\text{g/kg}$ given by either route of administration. These data are summarized in Table 2. Dilutions of 1:4, 1:8 and 1:16 offered partial protection to 20 $\mu\text{g/kg}$ of saxitoxin injected i.v., while only dilutions of 1:4 and 1:8 afforded mice protection from intratracheal instilled saxitoxin.

DISCUSSION

The purpose of our study was to assess whether passive immunization with anti-saxitoxin rabbit serum could protect mice against the lethal effects of saxitoxin given i.v. or by intratracheal instillation. Our investigation showed that rabbit antiserum was equally effective in protecting mice from challenge by either route of administration. The data also tend to confirm results previously reported by DAVTO (1965), who demonstrated protective effects of antiserum to s.c. injected saxitoxin. Thus, we have shown that

antiserum can protect mice from the lethal effects of saxitoxin administered either i.v. or by intratracheal instillation.

The data from this study also show that the lethal effects of saxitoxin can be manifested through respiratory exposure. Although the absorption kinetics of saxitoxin across the pulmonary epithelium were not measured directly in this study, the time to death and the similar LD₅₀s of intratracheally instilled and i.v. saxitoxin suggest a rapid absorption of the toxin from the respiratory tract to the circulatory system.

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TABLE 1. ACUTE TOXICITY OF SAXITOXIN TO MICE

<u>Intratracheal Instillation</u>		<u>Intravenous Injection</u>	
<u>Dose</u> <u>($\mu\text{g/kg}$)</u>	<u>#Dead/</u> <u>#Alive</u>	<u>Dose</u> <u>($\mu\text{g/kg}$)</u>	<u>#Dead/</u> <u>#Alive</u>
0 (control)	0/10	0 (control)	0/10
3.0	0/10	3.0	1/10
5.0	2/10	5.0	3/10
10.0	5/10	10.0	4/10
15.0	8/10	15.0	9/10
20.0	10/10	20.0	10/10
$\text{LD}_{50} = 11.2 \pm 0.6 \mu\text{g/kg}$		$\text{LD}_{50} = 11.7 \pm 0.4 \mu\text{g/kg}$	

TABLE 2. EFFECTS OF SAXITOXIN ANTISERUM ON LETHALITY OF SAXITOXIN*
ADMINISTERED EITHER INTRATRACHEALLY OR INTRAVENOUSLY

<u>Intratracheal Instillation</u>		<u>Intravenous Injection</u>	
<u>Antiserum dilution</u>	<u>#Dead/ #Alive</u>	<u>Antiserum dilution</u>	<u>#Dead/ #Alive</u>
1:1	0/9**	1:1	0/10
1:2	0/10	1:2	0/10
1:4	2/10	1:4	3/10
1:8	5/10	1:8	7/10
1:16	10/10	1:16	8/10
(1:32)	N.D.	1:32	10/10
Control serum	10/10	Control serum	10/10

* Saxitoxin dose = 20 µg/kg

** One animal died from trauma induced by the instillation procedure.